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REMARKS

Claims 36, 40, 41 and 44 have been amended. Claims 51-66 have been withdrawn from consideration as being directed to non-elected inventions. New claim 70 has been added. Thus, claims 36-70 are pending in the present application, with claims 36-50 and 67-70 currently under consideration. Support for the amendment to claim 36 may be found throughout the specification and in the Examples, for example at page 7, lines 14-20; and page 6, lines 6-9. The term "cross-linker" has been replaced with "cross-linking agent" in step (a) of claim 36 to maintain consistency with the language used in the description. Similarly, the term "epoxide" in claims 40, 41 and 44 has been replaced with "cross-linking agent" for consistency with the language used in the description. Support for new claim 70 may be found in claim 36, and throughout the specification and Examples. Thus, no new matter has been added. Reconsideration and withdrawal of the present objection and rejections in view of the remarks presented herein are respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 36-41, 46 and 47 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Zhao (WO 00/46253).

The previous amendment made to step (c) of claim 36, to specify that the cross-linked polysaccharide gel has "a single type of cross-linkage," was intended to convey that **one** type of cross-linkage was formed in the cross-linking step so as to form a cross-linked polysaccharide having cross-linkages that are of the same functional type, namely, ether bonds. In support of this amendment, the Examiner was referred to relevant sections of the specification and to passages in the cited art (e.g., Zhao) that described the formation of two or more different types of cross-linking bonds.

Nevertheless, the Examiner appears to have construed the term 'a single type of cross-linkage' to mean that the composition produced can have a given type of cross-linkage (e.g., double cross-link) which occurs as a result of achieving the method' (see page 13 of the Office Action). In other words, provided that the cross-linkages are all the same 'type' (e.g., 'all single' or 'all double'), the Examiner considers this would be 'a single type of cross-linkage'. The claims

have been amended to delete the offending phrase 'a single type of cross-linkage' from step (a) of claim 36.

Claim 36 as amended recites that the cross-linked polysaccharide produced according to the claimed process is one in which *"the cross-linking agent is substantially linked to the polysaccharide by ether bonds."* This process advantageously results in a cross-linked polysaccharide gel that is resistant to degradation.

In contrast, Zhao teaches cross-linking hyaluronic acid via **two or more different functional groups** (e.g., an ester and an ether, amide, imine, or amine – see page 4, lines 9-25; page 5, lines 11-21; page 6; page 7, lines 6-10; page 10, lines 20-25 of Zhao) so as to form two or more different cross-linking bonds. Furthermore, Zhao teaches that the formation of two or more different types of cross-linking bonds is required to achieve advantages such as high biostability (see page 4, lines 13-20 and page 13, line 26 to page 14, line 4).

Thus, Zhao does not teach (or suggest) a process for preparing a cross-linked polysaccharide gel that is resistant to degradation, and wherein the cross-linking agent is substantially linked to the polysaccharide by ether bonds, as recited in the present claims. Instead, Zhao teaches the formation of **at least two different cross-linking bonds** in order to produce a cross-linked polysaccharide that exhibits biostability. Accordingly, the present claims are not anticipated by Zhao.

In view of the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a)

Claims 36-50 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Zhao (WO 00/46253) in view of Målson (WO 87/07898).

As discussed above, the process taught by Zhao requires the formation of **two or more different cross-linking bonds** (e.g., an ester bond with an ether, amide, imino or amino bond – see page 5, lines 11-21 and page 6) by forming cross-linkages via two or more different functional groups (e.g., see page 4, lines 9-25; page 5, lines 11-21; page 7, lines 6-10; page 10, lines 20-25). Zhao explicitly teaches that the use of two or more different cross-linking bonds is required to achieve advantages such as high biostability (see page 4, lines 19-20 and page 13, line 28 to page 14, line 4). Furthermore, Zhao teaches that **the use or formation of two or more different**

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cross-linking bonds is superior to a cross-linked polysaccharide that is cross-linked by one cross-linking agent or having one functional bond. For example, page 13, line 25 to page 14, line 4 recites:

“In general a product according to the present invention has a greater degree of cross-linking, that is to say a denser network of cross-links than does single cross-linked HA. A higher degree of cross-linking has been found to reduce the water absorption capacity of the cross-linked HA, resulting in greater stability in aqueous solution. In addition double cross-linked HA has been found to exhibit greater stability against degradation by hyaluronidase, and against degradation due to free radicals, indicating an increased biostability.”

The term “double cross-linked HA” is defined on page 5, lines 3-10 of the specification to mean a hyaluronic acid derivative wherein a molecule of HA is cross-linked to another molecule of HA by means of **two different types of functional bonds**. Therefore, by disclosing that that the formation of two or more different cross-linking bonds (e.g., ester bonds and ether, amide, imino or amino bonds) is required for increased biostability, Zhao effectively teaches away from the presently claimed invention. Thus, in view of Zhao, one of ordinary skill in the art would not be motivated to cross-link hyaluronic acid by forming substantially only ether bonds, as opposed to two or more different types of functional bonds. In particular, one would certainly not use one cross-linking agent consisting essentially of a bifunctional epoxide or a polyfunctional epoxide, so as to produce a cross-linked polysaccharide wherein the cross-linking agent is substantially linked to the polysaccharide by one type of functional bond, namely ether bonds.

Målson discloses various reaction conditions for forming cross-linked polysaccharides, but does not disclose the claimed process. Even if the reaction conditions taught by Målson are combined with Zhao, the combined teaching would not lead one of ordinary skill in the art to the presently claimed invention because Zhao teaches that formation of two or more different cross-linking bonds is required to achieve biostability. Thus, the combination of Zhao and Målson provides no motivation for, and in fact teaches away from, a process for producing a cross-linked polysaccharide in which the cross-linking agent is substantially linked to the polysaccharide substantially by one type of functional bond, i.e., ether bonds.

Furthermore, in view of the teaching in Zhao that multiple types of functional bonds are required for biostability, it would not have been expected that a cross-linked polysaccharide

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produced according to the process of the instantly claimed invention would be resistant to degradation.

On page 10 of the Office Action, with regard to step (b) of claim 36, in which the cross-linking occurs during the drying step **without substantially removing epoxide from the alkaline medium**, the Examiner takes the view that the disclosure in Mälson that epoxide is removed **before the drying step** is within the scope of step (b). The applicants respectfully disagrees with this interpretation. Indeed, it is quite apparent from the language of steps (a) and (b) of claim 36 that the process does not involve removing excess epoxide from the alkaline medium until after the drying step has concluded. As acknowledged by the Examiner, Mälson explicitly teaches removing epoxide before the drying step. Accordingly, contrary to the Examiner's assertions, Mälson does not read on the present claims.

In view of the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

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CONCLUSION

Applicants submit that all claims are in condition for allowance. However, if minor matters remain, the Examiner is invited to contact the undersigned at the telephone number provided below. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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